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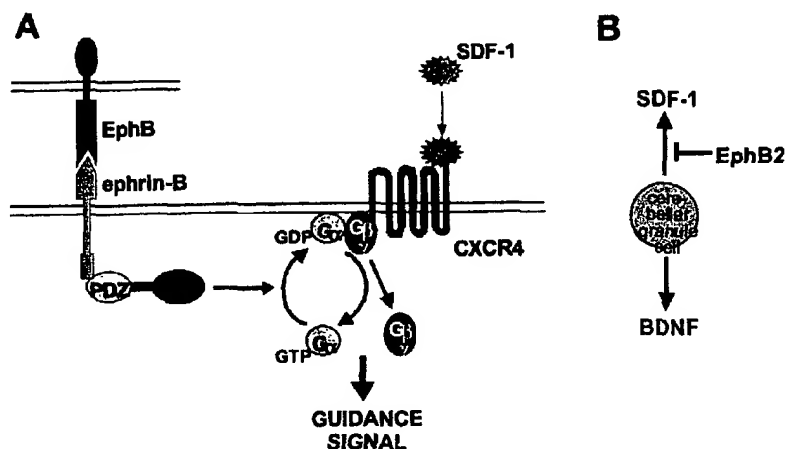
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(54) Title: B-EPHRIN REGULATION OF G-PROTEIN COUPLED CHEMOATTRACTION; COMPOSITIONS AND METHODS OF USE



(57) Abstract: Transmembrane B ephrins and their Eph receptors signal bi-directionally. The presently claimed invention describes a cytoplasmic protein, designated PDZ-RGS3, which binds B ephrins through a PDZ domain, and has a regulator of heterotrimeric G protein signaling (RGS) domain. PDZ-RGS3 mediates signaling from the ephrin-B cytoplasmic tail. SDF-1, a chemokine with a G protein coupled receptor, or BDNF, act as chemoattractants for cerebellar granule cells, with SDF-1 action being selectively inhibited by soluble EphB receptor. The claimed invention reveals a pathway that links reverse signaling to cellular guidance, uncovers a novel mode of control for G proteins, and demonstrates a mechanism for selective regulation of responsiveness to neuronal guidance cues. Further, compositions and methods of use are provided for modulating cell migration as a function of chemokines and GPCR interaction, to aid in the treatment of disease states and medical conditions, including cancer and immune responses such as allergy and autoimmune responses. In one embodiment, a method of altering the sensitivity of a cell to a chemokine is provided using a PDZ-RGS3 protein.

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